

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

**Claims 1-34.** (canceled)

**Claim 35.** (currently amended) A method of producing a zinc finger protein or a nucleic acid encoding the same, comprising:

(a) providing a database comprising designations for a plurality of precharacterized zinc finger proteins, each protein comprising at least first, second and third fingers, and subdesignations for each of the three fingers of each of the zinc finger proteins, wherein at least one protein in the database has a third finger that is different from the third finger of at least one other protein in the database; a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising at least first, second and third triplets specifically bound by the at least first, second and third fingers respectively in each zinc finger protein, the first, second and third triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first, second and third fingers are arranged in the zinc finger protein (N-terminal to C-terminal);

(b) providing a preselected target site for design of a new zinc finger protein, the target site comprising contiguous first, second and third triplets in a 3'-5' order,

(c) for the first, second and third triplet in the target site, identifying first, second and third sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising zinc finger protein(s) comprising a finger specifically binding to the second triplet in the target site, the third set comprising zinc finger protein(s) comprising a finger specifically binding to the third triplet in the target site;

(d) outputting designations and subdesignations of the zinc finger proteins in the first, second, and third sets identified in step (c); and

(e) producing (i) a new zinc finger protein that binds to the target site comprising a first finger from a zinc finger protein from the first set, a second finger from a zinc finger protein from the second set, and a third finger from a zinc finger protein from the third set, or (ii) a nucleic acid encoding the zinc finger protein.

**Claim 36.** (canceled)

**Claim 37.** (currently amended) A method of producing a zinc finger protein or nucleic acid encoding the same comprising:

(a) providing a database comprising designations for a plurality of precharacterized zinc finger proteins, each protein comprising at least first, second and third fingers, and subdesignations for each of the three fingers of each of the zinc finger proteins; a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising at least first, second and third triplets specifically bound by the at least first, second and third fingers respectively in each zinc finger protein, the first, second and third triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first, second and third fingers are arranged in the zinc finger protein (N-terminal to C-terminal);

(b) providing a preselected target site for design of a zinc finger protein, the target site comprising contiguous first, second and third triplets in a 3'-5' order,

(c) for the first, second and third triplet in the target site, identifying first, second and third sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising zinc finger protein(s) comprising a finger specifically binding to the second triplet in the target site, the third set comprising zinc finger protein(s) comprising a finger specifically binding to the third triplet in the target site;

~~The method of claim 35 further comprising~~ (d) identifying subsets of the first, second and third sets, the subset of the first set comprising zinc finger protein(s) comprising a finger that specifically binds to the first triplet in the target site from the first finger position of a zinc finger protein in the database; the subset of the second set comprising zinc finger protein(s) comprising a finger that specifically binds to the second triplet in the target site from the second finger position in a zinc finger protein in the database; the subset of the third set comprising zinc finger

protein(s) comprising a finger that specifically binds to the third triplet in the target site from a third finger position in a zinc finger protein in the database;

wherein

~~the outputting step comprises (e)~~ outputting designations and subdesignations of the subset of the first, second and third sets; and

~~the producing step comprises (f)~~ producing (i) a zinc finger protein comprising a first finger from the first subset, a second finger from the second subset, and a third finger from the third subset, or (ii) a nucleic acid encoding the same.

**Claim 38.** (original) The method of claim 37, wherein the outputting comprises outputting the designations and subdesignations of the subsets of the first, second and third sets, and the first, second and third sets minus their respective subsets.

**Claim 39.** (Canceled)

**Claim 40.** (original) The method of claim 35, wherein the target site is provided by user input.

**Claim 41.** (previously presented) The method of claim 35 wherein the target site is provided by

providing a target nucleic acid to be targeted by a zinc finger protein;  
selecting a plurality of potential target sites within the target nucleic acid sequence;  
evaluating whether each selected target site comprises 5'NNx aNy bNzc3; and  
outputting a selected target site within the target nucleic acid comprising 5'NNx aNy bNzc3', the output selected target site providing the target site in step (b) of claim 35, wherein each of (x, a), (y, b) and (z, c) is (N, N) or (G, K);  
at least one of (x, a), (y, b) and (z, c) is (G, K). and

N and K are IUPAC-IUB ambiguity codes.

**Claim 42.** (currently amended) A method of producing a zinc finger protein or a nucleic acid encoding the same, comprising:

(a) providing a database comprising

designations for a plurality of precharacterized zinc finger proteins, each protein comprising at least first and second fingers,

subdesignations for each of the fingers of each of the zinc finger proteins; and a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising first and second triplets specifically bound by the first and second fingers respectively, the triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first and second fingers are arranged in the zinc finger protein (N-terminal to C-terminal);

(b) providing a preselected target site for design of a new zinc finger protein, the target site comprising contiguous first and second triplets ordered 3'5' in the target site;

(c) for the first and second triplet in the target site, identifying first and second sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising zinc finger protein(s) comprising a finger specifically binding to the second triplet in the target site;

(d) identifying subsets of the first and second sets, the subset of the first set comprising zinc finger protein(s) comprising a finger that specifically binds to the first triplet in the target site from the first finger position of a zinc finger protein in the database; and the subset of the second set comprising zinc finger protein(s) comprising a finger that specifically binds to the second triplet in the target site from the second finger position in a zinc finger protein in the database;

~~(d)~~ (e) outputting designations and subdesignations of the zinc finger proteins in the subsets of the first, and second sets identified in step (c); and

~~(e)~~ (f) producing (i) a new zinc finger protein that binds to the target site comprising a first finger from a zinc finger protein from the subset of the first set and a second finger from a zinc finger protein from a subset of the second set, or (ii) a nucleic acid encoding the same.

**Claim 43.** (currently amended) A method of producing a zinc finger protein or a nucleic acid encoding the same, comprising:

(a) providing a database comprising:

designations for a plurality of precharacterized zinc finger proteins, each protein comprising at least first and second fingers;

subdesignations for each of the fingers of each of the zinc finger proteins; and  
a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising first, and second triplets specifically bound by the first and second fingers respectively, the triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first and second fingers are arranged in the zinc finger protein (N-terminal to C-terminal);

(b) providing a preselected target site for design of a new zinc finger protein, the target site comprising contiguous first, second and third triplets ordered 3'5' in the target site;

(c) for the first and third triplet in the target site, identifying first and second sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising zinc finger protein(s) comprising a finger specifically binding to the third triplet in the target site;

(d) identifying subsets of the first and second sets, the subset of the first set comprising zinc finger protein(s) comprising a finger that specifically binds to the first triplet in the target site from the first finger position of a zinc finger protein in the database; and the subset of the second set comprising zinc finger protein(s) comprising a finger that specifically binds to the third triplet in the target site from the second finger position in a zinc finger protein in the database;

~~(d)~~ (e) outputting designations and subdesignations of the subsets of the zinc finger proteins in the first and second sets identified in step (c); and

~~(e)~~ (f) producing (i) a new zinc finger protein that binds to the target site comprising first, second and third fingers, wherein the first finger is from a zinc finger protein from the subset of the first set and the third finger is from a zinc finger protein from the subset of the second set, or (ii) a nucleic acid encoding the same.

**Claims 44-47.** (canceled).

**Claim 48.** (currently amended) A computer program product for designing a zinc finger protein comprising:

(a) code for providing a database comprising

designations for a plurality of precharacterized zinc finger proteins, each protein comprising at least first, second and third fingers[[ ]], wherein at least one protein in the database has a third finger that is different from the third finger of at least one other protein in the database;

subdesignations for each of the three fingers of each of the zinc finger proteins;  
a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising at least first, second and third triplets specifically bound by the at least first, second and third fingers respectively in each zinc finger protein, the first, second and third triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first, second and third fingers are arranged in the zinc finger protein (N-terminus to C-terminus);

(b) code for providing a preselected target site for design of a new zinc finger protein, the target site comprising at least first, second and third triplets,

(c) for the first, second and third triplet in the target site, code for identifying first, second and third sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising zinc finger protein(s) comprising a finger specifically binding to the second triplet in the target site, the third set comprising zinc finger protein(s) comprising a finger specifically binding to the third triplet in the target site;

(d) code for outputting designations and subdesignations of the zinc finger proteins in the first, second, and third sets identified in step (c).

(e) a computer readable storage medium for holding the codes.

**Claim 49.** (currently amended) A system for designing a zinc finger protein comprising:

(a) a memory;

(b) a system bus;

(c) a processor operatively disposed to:

(1) provide a database comprising

designations for a plurality of precharacterized zinc finger proteins, each protein comprising at least first, second and third fingers, and subdesignations for each of the three



fingers of each of the zinc finger proteins; wherein at least one protein in the database has a third finger that is different from the third finger of at least one other protein in the database;

a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising at least first, second and third triplets specifically bound by the at least first, second and third fingers respectively in each zinc finger protein, the first, second and third triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first, second and third fingers are arranged in the zinc finger protein (N-terminus to C-terminus);

(2) provide or be provided with a preselected target site for design of a ~~new~~ zinc finger protein, the target site comprising at least first, second and third triplets,

(3) for the first, second and third triplet in the target site, identifying first, second and third sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising zinc finger protein(s) comprising a finger specifically binding to the second triplet in the target site, the third set comprising zinc finger protein(s) comprising a finger specifically binding to the third triplet in the target site;

(4) output designations and subdesignations of the zinc finger proteins in the first, second, and third sets identified in step (3).

**Claims 50-51.** (canceled)

**Claim 52.** (previously presented) The method of claim 35 wherein the target site is provided by

providing a polynucleotide sequence;

selecting a potential target site within the polynucleotide sequence; the potential target site comprising contiguous first, second and third triplets of bases at first, second and third positions in the potential target site;

determining a plurality of subscores by applying a correspondence regime between triplets and triplet position in a sequence of three contiguous triplets, wherein each triplet has first, second and third corresponding positions, and each combination of triplet and triplet position has a particular subscore

calculating a score for the potential target site by combining subscores for the first, second, and third triplets;

repeating the selecting, determining and calculating steps at least once on a further potential target site comprising first, second and third triplets at first, second and third positions of the further potential target site to determine a further score;

providing output of at least one potential target site with its score, the at least one output potential target site providing the preselected target site for step (b) in claim 35.

**Claim 53.** (currently amended) A computer implemented method of designing a zinc finger protein comprising:

(a) providing a database comprising designations for a plurality of precharacterized zinc finger proteins, each protein comprising at least first, second and third fingers, and subdesignations for each of the three fingers of each of the zinc finger proteins; wherein at least one third finger of the plurality of precharacterized zinc finger proteins is different from at least one other third finger; a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising at least first, second and third triplets specifically bound by the at least first, second and third fingers respectively in each zinc finger protein, the first, second and third triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first, second and third fingers are arranged in the zinc finger protein (N-terminal to C-terminal);

(b) providing a target site for design of a zinc finger protein, the target site comprising contiguous first, second and third triplets in a 3'-5' order,

(c) for the first, second and third triplet in the target site, identifying first, second and third sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising zinc finger protein(s) comprising a finger specifically binding to the second triplet in the target site, the third set comprising zinc finger protein(s) comprising a finger specifically binding to the third triplet in the target site;



(d) outputting designations and subdesignations of the zinc finger proteins in the first, second, and third sets identified in step (c).